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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,463	06/29/2001	A.K. Gunnar Aberg	559P019	6535

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EXAMINER	
JONES, DWAYNE C	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/895,463	ABERG, A.K. GUNNAR	
	Examiner	Art Unit	
	Dwayne C Jones	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-8 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-8 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/14/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-3, 6-8, and 11-17 are pending.

2. Claims 1-3, 6-8, and 11-17 are rejected.

Response to Arguments

3. Applicant's arguments and declaration filed on January 18, 2004 have been fully considered but they are not persuasive. Applicants present the following arguments. First, applicants allege that Johansson et al. of U.S. Patent No. 5,559,269 and Johansson et al. of U.S. Patent No. 5,686,464 do not teach or suggest that 5HM-TOLT, as well as DES-TOLT, are free from the side effect of QTc-prolongation, which is related to the cardiac arrhythmia of Torsades de pointes. Second, applicant argues that the Declaration of January 18, 2004 shows that positive in vivo effects of 5-HM tolterodine and DES-TOLT did not prolong the QTc interval in vivo.

4. First, applicants allege that Johansson et al. of U.S. Patent No. 5,559,269 and Johansson et al. of U.S. Patent No. 5,686,464 do not teach or suggest that 5HM-TOLT, as well as DES-TOLT, are free from the side effect of QTc-prolongation, which is related to the cardiac arrhythmia of Torsades de pointes. Both of these prior art references of Johansson et al. teach of the compounds of general formula I, (see column 1, lines 12-59 and column 2, lines 1-20), which are 3,3-diphenylpropylamine compounds. The 3,3-diphenylpropylamine compounds are known to be used to control urination, including urinary incontinence. In addition, these 3,3-diphenylpropylamine compounds, including

all of its metabolites, of Johansson et al. are present in the individual after administration. Accordingly, all metabolites are inherent with the administration of the compound of tolterodine, specifically including 5-hydroxymethyl-tolterodine and Des-isopropyl-tolterodine, see *Schering Corporation v Geneva Pharmaceuticals, Inc. and Novartis Corporation and Teva Pharmaceuticals Usa, Inc. and Andrx Corporation, Andrx Pharmaceuticals Llc and Andrx Pharmaceuticals, Inc. and Mylan Pharmaceuticals, Inc. and Wyeth, Esi-Lederle, Wyeth Pharmaceuticals, and Wyeth Consumer Healthcare (formerly American Home Products Corporation, Wyeth-Ayerst Laboratories, and Whitehall Robbins Healthcare) and IMPAX Laboratories, Inc. Apotex, Inc. And Novex Pharma, Copley Pharmaceutical, Inc. and GENPHARM, INC.* (CAFC, 02-1540,-1541,-1542,-1543,-1544,-1545,-1546,-1547,-1548,-1549, 03-1021,-1022,-1023,-1025,-1027, 8/1/2003).. Furthermore, even though the claims purport that there is a reduction or an elimination of concomitant liability of adverse side effects associated with the parent compounds, the courts have held, *In re Swinehart*, 169 USPQ 226, "a newly discovered property does not necessarily mean that the product is unobvious, since this property may be inherent in the prior art."

5. Second, applicant argues that the Declaration of January 18, 2004 shows that positive in vivo effects of 5-HM tolterodine and DES-TOLT did not prolong the QTc interval in vivo. Once the compounds of Johansson et al. of U.S. Patent No. 5,559,269 and Johansson et al. of U.S. Patent No. 5,686,464 are administered to an individual in need thereof these 3,3-diphenylpropylamine compounds will be metabolized by the body and the presence of these metabolites, as well as their properties, are inherent

with the administration of the 3,3-diphenylpropylamine compounds of Johansson et al. of U.S. Patent No. 5,559,269 and Johansson et al. of U.S. Patent No. 5,686,464, see *Schering Corporation v Geneva Pharmaceuticals, Inc. and Novartis Corporation and Teva Pharmaceuticals Usa, Inc. and Andrx Corporation, Andrx Pharmaceuticals Llc and Andrx Pharmaceuticals, Inc. and Mylan Pharmaceuticals, Inc. and Wyeth, Esi-Lederle, Wyeth Pharmaceuticals, and Wyeth Consumer Healthcare (formerly American Home Products Corporation, Wyeth-Ayerst Laboratories, and Whitehall Robbins Healthcare) and IMPAX Laboratories, Inc. Apotex, Inc. And Novex Pharma, Copley Pharmaceutical, Inc. and GENPHARM, INC.* (CAFC, 02-1540,-1541,-1542,-1543,-1544,-1545,-1546,-1547,-1548,-1549, 03-1021,-1022,-1023,-1025,-1027, 8/1/2003).

Information Disclosure Statement

6. The information disclosure statement filed originally on September 14, 2001 has been reviewed and considered, see enclosed copy of PTO FORM 1449.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3, 6-8, and 11-15 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Brynne et al. Brynne et al. disclose of the pharmacokinetics and

pharmacodynamics of tolterodine with its oral and intravenous dosages administration in man. In addition, Brynne et al. teach and identify the major metabolites of tolterodine, namely compound !!a (corresponds to instantly claimed 5-hydroxymethyl-tolterodine) and compound Ib (corresponds to instantly claimed Des-isopropyl-tolterodine), (see Figure 2 on page 291). Brynne et al. also teach that tolterodine is useful in the treatment of urinary bladder overactivity, (see abstract and page 288, 1st column, paragraphs 2 and 3). Once the compounds of Brynne et al. are administered to an individual in need thereof tolterodine compound will be metabolized by the body and the presence of these metabolites, as well as their properties, are inherent with the administration of tolterodine, see Schering Corporation v Geneva Pharmaceuticals, Inc. and Novartis Corporation and Teva Pharmaceuticals Usa, Inc. and Andrx Corporation, Andrx Pharmaceuticals Llc and Andrx Pharmaceuticals, Inc. and Mylan Pharmaceuticals, Inc. and Wyeth, Esi-Lederle, Wyeth Pharmaceuticals, and Wyeth Consumer Healthcare (formerly American Home Products Corporation, Wyeth-Ayerst Laboratories, and Whitehall Robbins Healthcare) and IMPAX Laboratories, Inc. Apotex, Inc. And Novex Pharma, Copley Pharmaceutical, Inc. and GENPHARM, INC. (CAFC, 02-1540,-1541,-1542,-1543,-1544,-1545,-1546,-1547,-1548,-1549, 03-1021,-1022,-1023,-1025,-1027, 8/1/2003).

9. The rejection of claims 6, 11, 12, 13, 14, 15, and 16 under 35 U.S.C. 102(b) as being clearly anticipated by Johansson et al. of U.S. Patent No. 5,559,269 is maintained for both the above-stated and reasons of record. Johansson et al. teach of the compounds of general formula I, (see column 1, lines 12-59 and column 2, lines 1-20).

Johansson et al. also teach that these compounds are used in the treatment of acetylcholine-mediated disorders, namely urinary incontinence. In addition, Johansson et al. disclose that a daily dosage from about 0.05 mg to about 200 mg daily, (see column 5, lines 55-65). Johansson et al. also teach of administering these compounds in various forms, namely oral and parenteral administration, (see column 5, lines 50-54). Even though the claims purport that there is a reduction or an elimination of concomitant liability of adverse side effects associated with the parent compounds, the courts have held, *In re Swinehart*, 169 USPQ 226, "a newly discovered property does not necessarily mean that the product is unobvious, since this property may be inherent in the prior art."

10. The rejection of claims 6, 11, 12, 13, 14, 15, and 16 under 35 U.S.C. 102(b) as being clearly anticipated by Johansson et al. of U.S. Patent No. 5,686,464 is maintained for both the above-stated and reasons of record. Johansson et al. teach of the compounds of general formula I when the variables of R^1, R^2, and R^3 each represent hydrogen and the variable of X represents $N(CH(CH_3)_2)_2$ and specifically the compound of Example 1, (see abstract, and columns 1-2, and column 6). Johansson et al. also teach that these compounds are used in the treatment of acetylcholine-mediated disorders, namely urinary incontinence. In addition, Johansson et al. disclose that a daily dosage from about 0.05 mg to about 200 mg daily, (see column 5, lines 55-65). In addition, Johansson et al. disclose of the optical isomers, the racemic mixture as well as the individual isomers as such, (see column 1, lines 57-59). Despite the fact that the claims purport that there is a reduction or an elimination of concomitant liability of

adverse side effects associated with the parent compounds, the courts have held, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable, see *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 1-3, 6-8, and 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claims 1-3, 6-8, and 11-15 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Brynne et al. Brynne et al. disclose of the pharmacokinetics and pharmacodynamics of tolterodine with its oral and intravenous dosages administration in man. In addition, Brynne et al. teach and identify the major metabolites of tolterodine, namely compound !!a (corresponds to instantly claimed 5-hydroxymethyl-tolterodine)

and compound Ib (corresponds to instantly claimed Des-isopropyl-tolterodine), (see Figure 2 on page 291). Brynne et al. also teach that tolterodine is useful in the treatment of urinary bladder overactivity, (see abstract and page 288, 1st column, paragraphs 2 and 3). Once the compounds of Brynne et al. are administered to an individual in need thereof tolterodine compound will be metabolized by the body and the presence of these metabolites, as well as their properties, are inherent with the administration of tolterodine, see Schering Corporation v Geneva Pharmaceuticals, Inc. and Novartis Corporation and Teva Pharmaceuticals Usa, Inc. and Andrx Corporation, Andrx Pharmaceuticals Llc and Andrx Pharmaceuticals, Inc. and Mylan Pharmaceuticals, Inc. and Wyeth, Esi-Lederle, Wyeth Pharmaceuticals, and Wyeth Consumer Healthcare (formerly American Home Products Corporation, Wyeth-Ayerst Laboratories, and Whitehall Robbins Healthcare) and IMPAX Laboratories, Inc. Apotex, Inc. And Novex Pharma, Copley Pharmaceutical, Inc. and GENPHARM, INC. (CAFC, 02-1540,-1541,-1542,-1543,-1544,-1545,-1546,-1547,-1548,-1549, 03-1021,-1022,-1023,-1025,-1027, 8/1/2003). Furthermore, the determination of pharmaceutically acceptable dosages as well as modes and methods of administration, such as rectal, sublingual or even controlled release preparations that have the optimum therapeutic amounts, are well within the purview of the skilled artisan. Accordingly, it would have been one having ordinary skill in the art at the time of the invention would have been motivated to develop pharmaceutically acceptable dosages and modes and methods of administration that have the optimum therapeutic amounts, are well within the purview of the skilled artisan.

14. The rejection of claims 1, 6, and 9-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. of U.S. Patent No. 5,686,464 is maintained for both the above-stated and reasons of record. Johansson et al. teach of the compounds of general formula I when the variables of R^1, R^2, and R^3 each represent hydrogen and the variable of X represent $N(CH(CH_3)_2)_2$ and a hydrocarbyl group, such as a methyl group, and specifically the compound of Example 1, (see abstract, and columns 1-2, and column 6). Moreover, Johansson et al. teach Johansson et al. also teach that these compounds is used in the treatment of acetylcholine-mediated disorders, namely urinary incontinence. In addition, Johansson et al. disclose that a daily dosage from about 0.05 mg to about 200 mg daily, (see column 5, lines 55-65). In addition, Johansson et al. disclose of the optical isomers, the racemic mixture as well as the individual isomers as such, (see column 1, lines 57-59). Despite the fact that the claims purport that there is a reduction or an elimination of concomitant liability of adverse side effects associated with the parent compounds, the courts have held, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable, see *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). It is well within the level of the skilled artisan to substitute a methyl group for a hydrogen atom. In this case, this compound, as claimed by applicant, would be a structural analog of the compounds disclosed by Johansson et al. One having ordinary skill in the art would have been motivated to select the claimed compound with the expectation that substitution of a methyl group for a hydrogen atom would not significantly alter the analogous properties of the compound of the reference

due to close structural similarity of the compounds. Accordingly, for those instant compounds that have a hydrogen atom in lieu of the prior art methyl group attached to the nitrogen atom, the skilled artisan would have been motivated to select these due to the close structural similarity.

15. The rejection of claims 1-3, 6-8, and 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. of U.S. Patent No. 6,313,132 for both the above-stated and reasons of record. Johansson et al. disclose of the diarylpropylamine compounds of general formula I for the treatment of urinary incontinence, (see columns 1 and 2, as well as column 4, lines 52-54). Due to the fact that the variable of R^4 is methyl as well as a hydroxymethyl group as well as the variables of R^6 and R^7 being equal to hydrocarbyl groups, such as methyl, one having ordinary skill in the art would have been motivated to select the claimed compound with the expectation that substitution of a methyl group for a hydrogen atom would not significantly alter the analogous properties of the compound of the reference due to close structural similarity of the compounds. Despite the fact that the claims purport that there is a reduction or an elimination of concomitant liability of adverse side effects associated with the parent compounds, the courts have held, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable, see *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Moreover, Johansson et al. teach Johansson et al. also teach that these compounds is used in the treatment of acetylcholine-mediated disorders, namely urinary incontinence.

In addition, Johansson et al. disclose that a daily dosage from about 0.05 mg to about 200 mg daily, (see column 9).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Thursday, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, may be reached at (571) 272-0584. The official fax No. for correspondence is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

DWAYNE JONES
PRIMARY EXAMINER
Tech. Ctr. 1614
April 21, 2004